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A potential of autologous pericardium for a sustained-release carrier of vancomycin: A pilot study in vitro

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Autologous pericardium has been widely used to repair destructed annuli in infective endocarditis complicated by annular abscess.[1,2] In the present study we investigated the in vitro property of autologous pericardium for a sustained-release carrier of vancomycin.

CLINICAL SUMMARY

Between January and May 2002, autologous pericardium with pericardial fat was harvested from the patients (n = 6) who underwent cardiac operations in our institute. After harvesting, the pericardium was cut into 7 pieces (1 cm × 1 cm each). Then 0.2 mL of vancomycin solution (15 mg/mL) was dropped onto each pericardium and incubated for 1 hour at room temperature so that the vancomycin solution was completely absorbed into the pericardium. The 7 pericardial patches with vancomycin were soaked in 7 test tubes containing 5 mL of saline, respectively. The test tubes were placed in the shaker and kept at 37°C. At 6 hours, 12 hours, and 1, 3, 5, 7, and 10 days after the incubation, the pericardium and the saline samples were collected and frozen from 1 of the 7 test tubes, and the saline in the residual test tubes were replaced with 5 mL of fresh saline (ie, the pericardia were left uncollected), respectively. We replaced the saline in the residual test tubes at each time point to maintain the diffusion gradient between the pericardium and the saline. To prevent the degradation of the samples, we froze them until the concentrations of vancomycin were measured. The vancomycin concentrations of the pericardium and the saline samples were measured as previously described.[3,4] We obtained written informed consent from each patient after a full explanation of this study. The protocol of this study complied with the principles set forth in the Helsinki Declaration.

All values are expressed as means ± standard deviations. Figure 1 shows that the percentage reaming of vancomycin in the pericardium at each time point was 67.8% ± 17.8%, 53.8% ± 12.3%, 37.8% ± 9.8%, 25.1% ± 10.1%, 12.6% ± 3.3%, 7.1% ± 3.1%, and 4.3% ± 1.7% for 6 hours, 12 hours, and 1, 3, 5, 7, and 10 days after the incubation, respectively. Figure 2 shows that the concentrations of vancomycin in the saline samples were 789 ± 143 μg/mL, 376 ± 56 μg/mL, 144 ± 23 μg/mL, 56 ± 14 μg/mL, 38 ± 5.2 μg/mL, 27 ± 3.8 μg/mL, and 15 ± 2.7 μg/mL for 6 hours, 12 hours, and 1, 3, 5, 7, and 10 days after the incubation, which were all greater than the minimum inhibitory concentration of vancomycin (2.0 μg/mL) against methicillin-resistant *Staphylococcus aureus* (MRSA). These results indicate that the pericardium can slowly release vancomycin and maintain the minimum inhibitory concentration of MRSA around the pericardium for more than 10 days.

DISCUSSION

In the present study we found that the autologous pericardium with fat might have a potential for a sustained-release carrier of vancomycin. Although this is an in vitro study and the mechanism of the sustained release was unclear, the property might help prevent prosthetic valve endocarditis by MRSA after reconstruction of the infected annulus.

Antibiotics are usually administrated systematically to prevent all forms of infection; however, this might be

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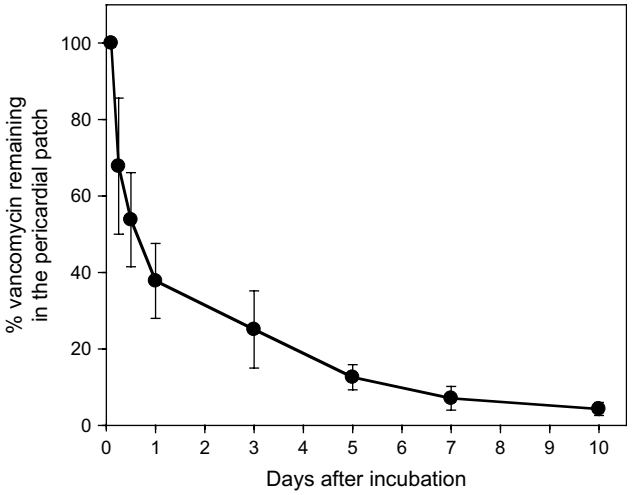

FIGURE 1. Release profile of vancomycin from the pericardium.

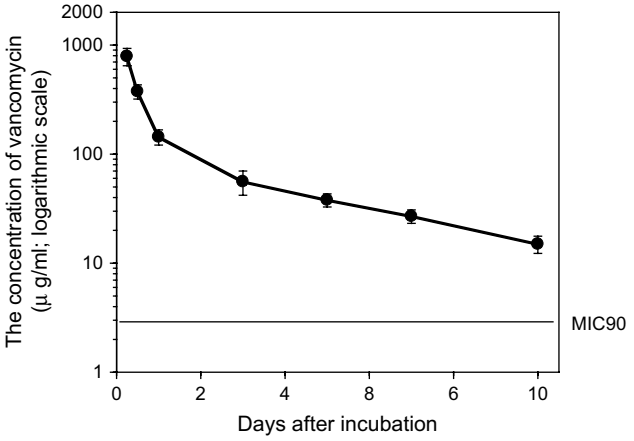

FIGURE 2. Concentration of vancomycin in the saline samples. *MIC*, Minimum inhibitory concentration.

insufficient to treat prosthetic valve endocarditis because the prosthesis directly contacts the infective sites.[1,2] Furthermore, maintenance of a sufficient blood concentration of antibiotics is sometimes difficult because prolonged systemic administration of high-dose antibiotics induces serious organ damage.

To avoid such disadvantages, we developed a local sustained-release system of vancomycin by using a poly-L-lactide-co-caprolactone sheet.[3,4] This sustained-release sheet of vancomycin drastically reduced the number of MRSA cells and prevented graft infection of the subcutis[3] and the abdominal aorta.[4] However, the fragile poly-L-lactide-co-caprolactone sheet cannot tolerate surgical manipulation and might cause thromboembolism if used in the cardiac cavity. On the other hand, autologous pericardium can be applied in several situations of cardiothoracic surgery, including annular reconstruction, and can be advantageous in terms of biocompatibility. However, it is difficult to know from the present data whether the same pericardial concentrations are maintained under more physiologic conditions. Thus further studies by large animals are required to determine the efficacy in vivo.

Fibrin glue has been applied as a carrier for vancomycin[5]; however, it can also cause serious thromboembolism. In addition, fibrin glue cannot release antibiotics for a sufficient period and the property of sustained release of vancomycin from the fibrin glue was not satisfactory compared with those of other antibiotics, such as teicoplanin and gentamicin.[5] We did not use glutaraldehyde for the preparation of pericardium to maintain its antibacterial and sustained-release properties.

In conclusion, autologous pericardium might have a potential for a sustained-release carrier of vancomycin. Further studies are required to determine the efficacy in vivo.

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